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ART UNIT	PAPER NUMBER
1654	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PTO-PAT-Email@rfem.com

Office Action Summary	Application No.	Applicant(s)	
	10/553,317	RUDOLPH ET AL.	
	Examiner	Art Unit	
	RONALD T. NIEBAUER	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 June 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-14,16-18 and 20-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-14,16-18 and 20-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/13/09; 7/15/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants amendments and arguments filed 6/10/09 are acknowledged and have been fully considered. Any rejection and/or objection not specifically addressed is herein withdrawn.

Previously (11/13/07) applicants elected thymosin alpha 1 as the alpha thymosin peptide, interferon alpha as the interferon, and PEG as the polymer. It is noted that newly added claim 23 does not expressly read on the elected species. However, since the rejections are applicable to claim 23, claim 23 has been included in the instant examination in order to advance prosecution.

Claims 2,15,19 have been cancelled.

Claims 1,3-14,16-18,20-23 are under consideration.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 8/13/09 has been considered.

The information disclosure statement filed 7/15/09 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered. No copy of the first NPL reference (i.e. Marcelo et al) has been provided.

Claim Rejections - 35 USC § 112

Claims were previously rejected under 112 2nd paragraph. Since claims have been amended and new claims added an updated rejection appears below.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1,3-6,10-14,16-18,23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 and dependent claims 3-6,10-14,16-18 refer to 'amino acid sequences substantially similar thereto and possess bioactivity substantially similar to that of naturally occurring TA1'. Claim 17 states 'peptide is substantially continuously maintained'. Claim 23 recites 'has bioactivity substantially similar to that of naturally occurring TA1'.

The terms 'substantially', 'substantially similar', 'substantially continuously' in claims 1,17,23 are relative terms which render the claims indefinite. The terms 'substantially' or 'substantially similar', or 'substantially continuously' are not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. In the instant case, the specification does not provide a specific definition of 'substantially' or 'substantially similar', or 'substantially continuously'. In paragraph 13, it is recited that modified sequences possess bioactivity substantially similar to that of TA1, e.g., a TA1 derived peptide having sufficient amino acid homology with TA1 such that it functions in substantially the same

way with substantially the same activity as TA1. However, such paragraph does not clearly set forth the metes and bounds of the claim. The term 'substantially similar' is described in terms of substantially the same. Such description does not provide a standard for ascertaining the scope of the claims. As such, the claim interpretation is dependent on ones subjective opinion.

Response to Arguments 112 2nd

Since the claims have been amended, a new rejection adapted to the claims is recited above.

Applicants argue that the term would have been understood by any person of ordinary skill in the art and that MPEP section 2173.05(b)(D) states that a term is definite when general guidelines are contained in the specification. Applicants argue that the general guidelines are at paragraph 13 of the specification.

Applicant's arguments filed 6/10/09 have been fully considered but they are not persuasive.

Although Applicants argue that the term would have been understood by any person of ordinary skill in the art and that MPEP section 2173.05(b)(D) states that a term is definite when general guidelines are contained in the specification, the instant specification does not provide such guidelines. In paragraph 13, it is recited that modified sequences possess bioactivity substantially similar to that of TA1, e.g., a TA1 derived peptide having sufficient amino acid homology with TA1 such that it functions in substantially the same way with substantially the same activity as TA1. However, such paragraph does not clearly set forth the metes and bounds of the claim. The term 'substantially similar' is described in terms of substantially the same.

Such description does not provide a standard for ascertaining the scope of the claims. It is noted that the claims refer to amino acid sequences that are 'substantially similar'. However, no direction is provides as to whether the sequences are similar in length, molecular weight, name, hydrophobicity, etc. Further, there is no direction provides as to what similarity is required for a sequence to be considered 'substantially similar'. As such, the claim interpretation is dependent on ones subjective opinion.

Claims were previously rejected under 112 1st paragraph – written description. Since the claims have been amended an updated rejection appears below.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1,3-6,10-14,16-18,23 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, as of the filing date of the application, of the specific subject matter later claimed by him. The courts have stated:

> "To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997); In re Gostelli, 872 F.2d 1008,

> 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966." Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

Further, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In *Regents of the University of California v. Eli Lilly & Co.* the court stated:

> "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *Fiers*, 984 F.2d at 1171, 25 USPQ2d 1601; *In re Smythe*, 480 F.2d 1376, 1383, 178 USPQ 279, 284985 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus …") *Regents of the University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398.

The MPEP further states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP § 2163. The MPEP does state that for a generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. MPEP § 2163. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See MPEP § 2163. Although the MPEP does not define what constitute a sufficient number of representative species, the courts have indicated what do not constitute a representative number of species to adequately describe a broad generic. In *Gostelli*, the courts

determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. *In re Gostelli*, 872, F.2d at 1012, 10 USPQ2d at 1618.

The MPEP lists factors that can be used to determine if sufficient evidence of possession has been furnished in the disclosure of the Application. These include "level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient." MPEP § 2163. While all of the factors have been considered, a sufficient amount for a *prima facie* case are discussed below.

Further, to provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include: a) the scope of the invention; b) actual reduction to practice; c) disclosure of drawings or structural chemical formulas; d) relevant identifying characteristics including complete structure, partial structure, physical and/or chemical properties, and structure/function correlation; e) method of making the claimed compounds; f) level of skill and knowledge in the art; and g) predictability in the art.

In the instant case, the claims are drawn to methods of treatment comprising administering an alpha thymosin peptide selected from a group including (claims 1,23) substituted, deleted, elongated, or replaced or abbreviated amino acid sequences wherein the sequences are substantially similar to and possess bioactivity substantially similar to that of naturally occurring TA1.

Although unclear (see 112 2nd) for purposes of examination the term 'substantially' has been given its broadest reasonable interpretation. It is noted that claims 7-9,20-22 are not included in the instant rejection since they refer to specific unmodified TA1 peptides.

(1) Level of skill and knowledge in the art/predictability in the art:

The level of skill in the art is high. There is unpredictability in predicting functional effects of abbreviated sequences and of substituted, deleted, elongated, or replaced sequences. It is not within the skill of the art to predict any and all substitutions, deletions, elongations, or replacements or abbreviations that would result in peptides possessing substantially similar bioactivity. The art recognizes that structure is not necessarily a reliable indicator of function.

(2) Scope of the invention/Partial structure/disclosure of drawings:

In the instant case, the claims are drawn to methods of treatment comprising administering an alpha thymosin peptide selected from a group including (claims 1,23) substituted, deleted, elongated, or replaced or abbreviated amino acid sequences wherein the sequences are substantially similar to and possess bioactivity substantially similar to that of naturally occurring TA1.

Although unclear (see 112 2nd) for purposes of examination the term 'substantially' has been given its broadest reasonable interpretation.

In considering the size of the genus of TA1 peptides with replacements, if one considered sequences in which 20 amino acids of thymosin alpha 1 (which is 28 amino acids long) were substituted with any of the 20 naturally occurring amino acids there would be at least 20^{20} (i.e. 104857600000000000000000000) different peptides in the genus or replacements. Absent a structure/function correlation it is unclear which peptides would possess the claimed bioactivity.

Further, there are many other deleted or elongated or abbreviated peptides. Hence, there is substantial variability in the genus.

No specific examples other than naturally occurring TA1 are provided in the specification. It is noted that claim 7 is limited to thymosin alpha 1 and is not included in the instant rejection. No specific examples are provided of substituted, deleted, or elongated or abbreviated sequences. Since there are a substantial variety of polypeptides possible within the genus, the examples do not constitute a representative number of species and do not sufficiently describe the genus claimed (see Gostelli above). One of skill in the art would not recognize that applicant was in possession of the claimed genus.

(3) Physical and/or chemical properties and (4) Functional characteristics:

The claims recite that the alpha thymosin peptide is to be useful for treating respiratory coronavirus infection or SARS. The claims state that the peptides possess bioactivity substantially similar to naturally occurring TA1. There is no correlation provided between function and structure. No direction is provided as to what core sequence is necessary to treat respiratory coronavirus infection or SARS. No direction is provided as to the relevant bioactivity that is necessary to perform the claimed function. In particular, there are no common structural attributes that identify the members of the genus. There is no teaching in the specification regarding which/how many residues of the structure can be varied while retaining the ability to treat respiratory coronavirus infection or SARS and possess bioactivity substantially similar to naturally occurring TA1. There is no disclosure relating similarity of structure to conservation of function. One of skill in the art would not recognize which peptides would be useful for treating respiratory coronavirus infection or SARS and possess bioactivity substantially similar to

naturally occurring TA1. Thus, one skilled in the art would not conclude that the applicant was in possession of the claimed genus.

(5) Method of making the claimed invention:

No examples are provided. The specification refers to other documents involving the use of the TA1 peptide (section 0026).

As stated *supra*, the MPEP states that written description for a genus can be achieved by a representative number of species within a broad generic. It is unquestionable that claim(s) 1 and dependent claims 3-6,10-14,16-18,23 is/are broad and generic, with respect to all possible peptides encompassed by the claims. The possible structural variations are many. Although the claims may recite some functional characteristics, the claims lack written description because there is no disclosure of a correlation between function and structure of the polypeptides beyond those polypeptides specifically disclosed in the examples in the specification. Moreover, the specification lacks sufficient variety of species to reflect this variance in the genus. While having written description of polypeptides identified in the specification tables and/or examples, the specification does not provide sufficient descriptive support for the myriad of polypeptides embraced by the claims.

The description requirement of the patent statue requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See *In re Wilder*, 736, F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate.") Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of the claims and

does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

Response to Arguments 112 1st written description

Since the claims have been amended, a new rejection adapted to the claims is recited above.

Applicants argue that the claims have been amended.

Applicants argue that it is not reasonable to interpret the sequence to include numerous peptides that have no amino acids in common with TA1 as substantially similar.

Applicants argue that the bioactivity of TA1 is well-known in the art. Applicants argue that the person of skill would easily conclude that peptides close enough in structure fall within the invention.

Applicants argue that methods of making are not a fair basis for a rejection.

Applicants submit that the correlation between structure and function is between substantial similarity in structure and the bioactivity of TA1 and the inventive method.

Applicant's arguments filed 6/10/09 have been fully considered but they are not persuasive.

Although Applicants argue that the claims have been amended, an updated rejection adapted to the instant claim set is set forth above.

Although Applicants argue that it is not reasonable to interpret the sequence to include numerous peptides that have no amino acids in common with TA1 as substantially similar, the instant claims recite 'amino acids substantially similar'. There is no specificity as to whether the

sequences are similar in length, molecular weight, name, hydrophobicity, etc. Further, there is no direction provided as to what similarity is required for a sequence to be considered 'substantially similar'. In accord with section 2111 of the MPEP the claims are given the broadest reasonable interpretation. As such, amino acid sequences that are similar in length are considered 'substantially similar', for example. As discussed above, in considering the size of the genus of TA1 peptides with replacements, if one considered sequences in which 20 amino acids of thymosin alpha 1 (which is 28 amino acids long) were substituted with any of the 20 naturally occurring amino acids there would be at least 20^{20} (i.e. 1048576000000000000000000000) different peptides in the genus or replacements. Absent a structure/function correlation it is unclear which peptides would possess the claimed bioactivity. Further, there are many other deleted or elongated or abbreviated peptides. Hence, there is substantial variability in the genus.

Although Applicants argue that the bioactivity of TA1 is well-known in the art, a function (or activity) is not the equivalent of a structure/function correlation. As discussed above, instant claim 7 is not rejected under 112 written description. As such, the issue is not TA1. The claims refer to alpha thymosin peptide selected from a group including (claims 1,23) substituted, deleted, elongated, or replaced or abbreviated amino acid sequences wherein the sequences are substantially similar to and possess bioactivity substantially similar to that of naturally occurring TA1. Although applicants assert the function of TA1 is well-known, no specific references have been cited to support such a position. Even if references were cited regarding the function alone, it is noted that a disclosure of a function does not necessarily provide direction as to what core sequence is necessary to treat respiratory coronavirus infection or SARS. The art recognizes that structure is not necessarily a reliable indicator of function. In the instant case, no direction is

provided as to the relevant bioactivity that is necessary to perform the claimed function. In particular, there are no common structural attributes that identify the members of the genus. There is no teaching in the specification regarding which/how many residues of the structure can be varied while retaining the ability to treat respiratory coronavirus infection or SARS and possess bioactivity substantially similar to naturally occurring TA1.

Although Applicants argue that the person of skill would easily conclude that peptides close enough in structure fall within the invention, it is noted that the instant claims are rejected under 112 2nd paragraph as discussed above. Applicants assertion that peptides "close enough" in structure is evidence that the claim interpretation is dependent on ones subjective opinion. In other words, the specification does not provide a standard for ascertaining 'substantially similar' peptides nor 'close enough' peptides. In the instant case, there is no disclosure relating similarity of structure to conservation of function. One of skill in the art would not recognize which peptides would be useful for treating respiratory coronavirus infection or SARS and possess bioactivity substantially similar to naturally occurring TA1. Thus, one skilled in the art would not conclude that the applicant was in possession of the claimed genus.

Although Applicants argue that methods of making are not a fair basis for a rejection, section 2163 II A 3(a)(i) of the MPEP states :

"Factors to be considered in determining whether there is sufficient evidence of possession include the level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention." Thus, method of making the claimed invention is a fair consideration in making a rejection.

Although Applicants submit that the correlation between structure and function is between substantial similarity in structure and the bioactivity of TA1 and the inventive method, such statement is confusing. The claims recite that the alpha thymosin peptide is to be useful for treating respiratory coronavirus infection or SARS. The claims state that the peptides possess bioactivity substantially similar to naturally occurring TA1. There is no correlation provided between function and structure. No direction is provided as to what core sequence is necessary to treat respiratory coronavirus infection or SARS. No direction is provided as to the relevant bioactivity that is necessary to perform the claimed function. In particular, there are no common structural attributes that identify the members of the genus. There is no teaching in the specification regarding which/how many residues of the structure can be varied while retaining the ability to treat respiratory coronavirus infection or SARS and possess bioactivity substantially similar to naturally occurring TA1. There is no disclosure relating similarity of structure to conservation of function. One of skill in the art would not recognize which peptides would be useful for treating respiratory coronavirus infection or SARS and possess bioactivity substantially similar to naturally occurring TA1. Thus, one skilled in the art would not conclude that the applicant was in possession of the claimed genus.

Claims were previously rejected under 112 1st paragraph – enablement. Since the claims have been amended and new claims added an updated rejection appears below.

Claims 1,3-14,16-18,20-23 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not

described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

> The factors to be considered in determining whether a disclosure meets the enablement requirements of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir., 1988). The court in Wands states, "Enablement is not precluded by the necessity for some experimentation, such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue', not 'experimentation'" (*Wands*, 8 USPQ2sd 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations" (*Wands*, 8 USPQ2d 1404). Among these factors are: (1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

While all of these factors are considered, a sufficient amount for a *prima facie* case is discussed below.

(1) The nature of the invention:

The claims are drawn to methods of treating a patient with a respiratory coronavirus infection, one who has had contact with a SARS carrier or an asymptomatic SARS carrier (claim 1). The claims specifically refer to those with SARS (claim 3). The agent used for treatments includes an alpha thymosin peptide selected from a group including (claims 1,23) substituted, deleted, elongated, or replaced or abbreviated amino acid sequences wherein the sequences are substantially similar to and possess bioactivity substantially similar to that of naturally occurring TA1. Although unclear (see 112 2nd) for purposes of examination the term 'substantially' has been given its broadest reasonable interpretation.

(3) The state of the prior art and (4) the predictability or unpredictability of the art:

The state of the art in treating coronavirus infection such as SARS is unpredictable. First it is noted that section 2164.05(a) states that the state of the prior art is the state at the time the application was filed. In the instant case, applicant claims benefit of provisional applications dating to 4/23/03. Thus the state of the art is considered as of 4/23/03. It is noted that there is limited literature available on the art up to 4/23/03. In the instant case, post-filing date references are cited to show the unpredictability in the art after the filing date.

Holmes (Journal of Clinical Investigation 2003 11:1605-1609; first cited with office action dated 12/28/07) state that (page 1607 2nd column first full paragraph) there are no approved antiviral drugs that are highly effective against coronaviruses. On page 1608 (last paragraph) Holmes states that 'development of effective drugs and vaccines for SARS is likely to take a long time'. Holmes states that 'The SARS epidemic appears to be out of control in some areas....it now appears likely that drugs and/or vaccines will be needed to control the epidemic' (page 1608 last paragrpah). As such, the state of the art in treating SARS and other ailments caused by coronavirus is unpredictable

Fujii et al. (J Infect Chemother 2004 10:1-7; first cited with office action dated 12/28/07) summarize clinical reports of attempted treatment of SARS. Fujii et al. state (page 1 column 2 line 17) that 'the treatment of SARS remains largely anecdotal, and no treatment consensus has yet been reached'. In the same paragraph Fujii et al. state that 'until we have efficacious vaccines and specific anti-SARS-CoV agents, SARS is likely to remain a major health threat to the world'. As such, the state of the art in treating SARS is unpredictable.

Stockman et al., (PLOS Medicine v3 issue 9 Sept 2006 pages 1525-1531; first cited with office action dated 2/18/09) teach a systematic review of treatments of SARS (page 1525).

Stockman teach that sources of the data included numerous databases and include data up to February 2005 (page 1525). Stockman conclude 'it was not possible to determine whether treatments benefited patients during the SARS outbreak. Some may have been harmful' (page 1525). As such, the state of the art in treating SARS is unpredictable.

The Merck Manual (on-line version www.merck.com/mmhe severe acute respiratory syndrome entry accessed Dec 2007; first cited with office action dated 12/28/07) teach (last paragraph) that doctors may treat SARS with drugs. 'However, there is no evidence that these or any other drugs are effective'. Further (last sentence), it is stated that effective treatments and preventative vaccines are still in the research stage. As such, the state of the art in treating SARS is unpredictable even as of 2007.

Taken together, the art teach that the treatment of SARS is unpredictable.

(5) The relative skill of those in the art:

The level of skill in the art is high. There is unpredictability in predicting functional effects of abbreviated sequences and of substituted, deleted, elongated, or replaced or abbreviated sequences. It is not within the skill of the art to predict any and all substitutions, deletions, elongations, or replacements or abbreviations that would result in peptides possessing substantially similar bioactivity. The art recognizes that structure is not necessarily a reliable indicator of function.

(2) The breadth of the claims

The claims are drawn to methods of treating a patient with a respiratory coronavirus infection, one who has had contact with a SARS carrier or an asymptomatic SARS carrier (claim

1). The claims specifically refer to those with SARS (claim 3). The agent used for treatments includes an alpha thymosin peptide selected from a group including (claims 1,23) substituted, deleted, elongated, or replaced or abbreviated amino acid sequences wherein the sequences are substantially similar to and possess bioactivity substantially similar to that of naturally occurring TA1. Although unclear (see 112 2nd) for purposes of examination the term 'substantially' has been given its broadest reasonable interpretation.

In addition to SARS, Holmes teach (page 1605 2nd column first complete paragraph) that coronaviruses are known as the cause of certain colds. Holmes teach (page 1605 last paragraph) that coronaviruses cause diseases in livestock, poultry and rodents. In addition to SARS, Holmes recites numerous other coronaviruses (page 1606 first column) including FIPV,HEV,IBV,MHV,and TGEV for example.

(6) The amount of direction or guidance presented and (7) the presence or absence of working examples:

The specification is void of any working examples. The specification (section 0016) states that contemplated treatments include immune-stimulating-effective amounts of the TA1 peptide. Applicants refer to prior art involving conjugating peptides to polymers (section 0025) and use of the TA1 peptide (section 0026). However, a correlation or evidence that immune-stimulation is adequate for treatment of SARS has not been provided. In fact, the teachings of Holmes, Fujii, Stockman, and The Merck Manual show unpredictability in the art for a wide range of agents.

One of skill in the art would not equate the asserted immune stimulating activity of TA1 with the ability to treat any and all coronavirus infections. Further, the specification does not

provide any correlation between TA1 and their ability to treat any and all coronavirus infections. Such guidance is necessary because the prior art cited above teach that the treatment of coronavirus infections such as SARS is unpredictable. Accordingly one would be burdened with undue experimentation to determine if the peptides of the current invention could be used in methods of prevention or treatment.

It is noted that section 2164.02 of the MPEP states that working examples are factors to be considered especially for undeveloped arts. In the instant case since there is very little literature about treating SARS prior to the filing of the instant application, the treatment of SARS is considered an undeveloped art.

It is noted that section 2164.03 of the MPEP states that the amount of guidance is inversely related to the state and predictability in the art. As evidenced by the teachings of Holmes, Fujii, Stockman, and The Merck Manual, treating SARS is highly unpredictable.

(8) The quantity of experimentation necessary:

Experimentation is required in numerous areas particularly related to how to use the method and determination if it would be useful for the treatment of coronavirus infections especially SARS. The claims are drawn to methods of treating a patient with a respiratory coronavirus infection, one who has had contact with a SARS carrier or an asymptomatic SARS carrier (claim 1). The claims specifically refer to those with SARS (claim 3). The agent used for treatments includes an alpha thymosin peptide selected from a group including (claims 1,23) substituted, deleted, elongated, or replaced or abbreviated amino acid sequences wherein the sequences are substantially similar to and possess bioactivity substantially similar to that of naturally occurring TA1. Although unclear (see 112 2nd) for purposes of examination the term

'substantially' has been given its broadest reasonable interpretation. In considering the size of the genus of TA1 peptides with replacements (claims 1,3-6,10-14,16-18), if one considered sequences in which 20 amino acids of thymosin alpha 1 (which is 28 amino acids long) were substituted with any of the 20 naturally occurring amino acids there would be at least 20^{20} (i.e. 104857600000000000000000000) different peptides in the genus or replacements. Absent a structure/function correlation it is unclear which peptides would possess the claimed bioactivity. Further, there are many other deleted or elongated or abbreviated peptides. Hence, there is substantial variability in the genus. Experimentation would be required to determine which, if any, of the peptides would have the claimed function. Considering the state of the art as discussed by the references above, particularly with regards to the high unpredictability in the art as evidenced therein, and the lack of guidance provided in the specification, one of ordinary skill in the art would be burdened with undue experimentation to practice the invention commensurate in the scope of the claims.

Response to Arguments 112 1st enablement

Since the claims have been amended, a new rejection adapted to the claims is recited above.

Applicants argue that the claims have not been fairly and reasonably interpreted.

Applicants argue that the art cited by the examiner is not relevant.

Applicants argue that TA1 is not an antiviral agent. Applicants argue that the references only demonstrate the importance of the invention.

Applicants argue that the authors of the publications were not aware of the present teachings.

Applicants argue that working examples are not relevant.

Applicants argue that experimentation is not undue.

Applicant's arguments filed 6/10/09 have been fully considered but they are not persuasive.

Although Applicants argue that the claims have not been fairly and reasonably interpreted, in accord with section 2111 of the MPEP the claims are given the broadest reasonable interpretation. As discussed above (112 2nd) the terms 'substantially', 'substantially similar', 'substantially continuously' in claims 1,17,23 are relative terms which render the claims indefinite. There is no specificity as to whether the sequences are similar in length, molecular weight, name, hydrophobicity, etc. Further, there is no direction provided as to what similarity is required for a sequence to be considered 'substantially similar'. As such, amino acid sequences that are similar in length are considered 'substantially similar', for example.

Although Applicants argue that the art cited by the examiner is not relevant, it is noted that the factors to be considered in determining whether a disclosure meets the enablement requirements of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir., 1988). The court in Wands states, "Enablement is not precluded by the necessity for some experimentation, such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue', not 'experimentation'" (*Wands*, 8 USPQ2sd 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the

invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations" (*Wands*, 8 USPQ2d 1404). Among these factors are: (1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary. In the instant case, the claims are drawn to methods of treating a patient with a respiratory coronavirus infection, one who has had contact with a SARS carrier or an asymptomatic SARS carrier (claim 1). As such, the art cited relating to treatment of SARS, for example, is relevant to the predictability or unpredictability of the art.

Although Applicants argue that TA1 is not an antiviral agent, such argument supports the position that the claims are not enabled. The claims are drawn to treating a coronavirus infection. Since applicants state on the record that TA1 is not antiviral one would not expect TA1 to be effective as claimed.

Although Applicants argue that the references only demonstrate the importance of the invention, it is noted that the factors to be considered in determining whether a disclosure meets the enablement requirements of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir., 1988). The court in Wands states, "Enablement is not precluded by the necessity for some experimentation, such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue', not 'experimentation'" (*Wands*, 8 USPQ2sd 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of

experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations" (*Wands*, 8 USPQ2d 1404). Among these factors are: (1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary. In the instant case, the claims are drawn to methods of treating a patient with a respiratory coronavirus infection, one who has had contact with a SARS carrier or an asymptomatic SARS carrier (claim 1). As such, the art cited relating to treatment of SARS, for example, is relevant to the unpredictability of the art.

Although Applicants argue that the authors of the publications were not aware of the present teachings, such information is an assertion and does not alter the state of the art at the time of the invention. As noted above, the state of the art in treating coronavirus infection such as SARS is unpredictable. It is noted that section 2164.05(a) states that the state of the prior art is the state at the time the application was filed. In the instant case, applicant claims benefit of provisional applications dating to 4/23/03. Thus the state of the art is considered as of 4/23/03. It is noted that there is limited literature available on the art up to 4/23/03. In the instant case, post-filing date references are cited to show the unpredictability in the art after the filing date.

Although Applicants argue that working examples are not relevant, it is noted that the factors to be considered in determining whether a disclosure meets the enablement requirements of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir., 1988). The court in Wands states, "Enablement is not precluded by the

necessity for some experimentation, such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue', not 'experimentation'" (*Wands*, 8 USPQ2sd 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations" (*Wands*, 8 USPQ2d 1404). Among these factors are: (1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary. In the instant case, the prior art teach unpredictability in treating SARS for example. It is noted that section 2164.02 of the MPEP states that working examples are factors to be considered especially for undeveloped arts. In the instant case since there is very little literature about treating SARS prior to the filing of the instant application, the treatment of SARS is considered an undeveloped art.

Although Applicants argue that experimentation is not undue, the court in Wands states, "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations" (*Wands*, 8 USPQ2d 1404). Among these factors are: (1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary. In the instant case, the

factors have been discussed above. Considering the state of the art as discussed by the references above, particularly with regards to the high unpredictability in the art as evidenced therein, and the lack of guidance provided in the specification, one of ordinary skill in the art would be burdened with undue experimentation to practice the invention commensurate in the scope of the claims.

Conclusion

Applicants addition of new claims 20-23 and amendments to claim 1 have necessitated any new rejections.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to RONALD T. NIEBAUER whose telephone number is (571)270-

3059. The examiner can normally be reached on Monday-Thursday, 7:30am-5:00pm, alt. Friday, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Anish Gupta/
Primary Examiner, Art Unit 1654

/Ronald T Niebauer/
Examiner, Art Unit 1654